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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,044	09/09/2004	Takahito Hara	3033 USOP	8870

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TAKEDA PHARMACEUTICALS NORTH AMERICA, INC  
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EXAMINER
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CORDERO GARCIA, MARCELA M

ART UNIT	PAPER NUMBER
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1654

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/30/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/507,044	<b>Applicant(s)</b> HARA ET AL.	
	<b>Examiner</b> Marcela M. Cordero Garcia	<b>Art Unit</b> 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 18 January 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 5 and 11-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/04</u> .   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1-33 are pending in the application.

#### ***Election/Restrictions***

Applicant's election of Group I, claims 1-10 in the reply filed on January 18, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In addition, Applicant elected the preparation of Example 3, comprising leuprorelin acetate and testosterone as the species.

Claims 5 and 11-33 are withdrawn as not drawn to the elected group or species.

Claims 1-4 and 6-10 are presented for examination.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 6-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by

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structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

***In the instant case, the claims are drawn to a pharmaceutical agent comprising 1) an LHRH receptor agonist or antagonist or a salt thereof in combination with 2) an androgen receptor agonist or a salt thereof. The claims are also drawn to an agent for the prophylaxis or treatment of hormone-dependent disease.*** In regards to the "LHRH receptor agonist or antagonist" term, this is a very broad generic statement drawn any agonist or antagonist of LHRH, there

exists a plethora of such compounds, which are not adequately described and/or represented in the examples drawn only to peptidic embodiments (pages 9-14). By the same token, the terms "androgen receptor agonist" are exemplified in page 15, lines 5-13. The claims are drawn, not only to the instant compositions, but to those with prophylactic and therapeutic activity for any kind of hormone-dependent disease, such as prostate cancer, uterine cancer, breast cancer, pituitary gland tumor and the like, prostatic hypertrophy, endometriosis, hysteromyoma, precocious puberty, dysmenorrheal, amenorrhea, premenstrual syndrome, multilocular ovarian syndrome, postoperative recurrence of the aforementioned cancers, dwarfism, Alzheimer's disease, climacteric disturbance, indefinite complaints, metastasis of the aforementioned cancers, calcium phosphorus bone metabolism disorder, contraception (or infertility when a rebound effect after drug withdrawal is utilized, benign or malignant tumor which is sex hormone non dependent but LHRH sensitive (page 18, lines 17-30) therefore a mere statement that such compounds would be desirable for treating all those diseases does not sufficiently provide ample written description.

The specification does provide examples of what qualify as compounds of the claimed invention (see, e.g, disclosure, 9-15), however, the examples are drawn only to leuporelin with testosterone (pages 68-70). As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is a broad generic with respect all possible compounds encompassed by the claims. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims

may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of combinations with e.g., non-peptidic LHRH agonists or antagonists or non-steroidal androgen receptor agonists. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claims 6-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims encompass using the claimed compounds to prevent a hormone-dependent disease such as prostate cancer, uterine cancer, breast cancer, pituitary gland tumor and the like, prostatic hypertrophy, endometriosis, hystero myoma, precocious puberty, dysmenorrheal, amenorrhea, premenstrual syndrome, multilocular ovarian syndrome, postoperative recurrence of the aforementioned cancers, dwarfism, Alzheimer's disease, climacteric disturbance, indefinite complaints, metastasis of the aforementioned cancers, calcium phosphorus

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bone metabolism disorder, contraception (or infertility when a rebound effect after drug withdrawal is utilized, benign or malignant tumor which is sex hormone non dependent but LHRH sensitive (page 18, lines 17-30), which is clearly beyond the scope of the instantly disclosed/claimed invention. Please note that the term "prevent" is an absolute definition, which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes) – including preventing such disorders as hormone-dependent disease such as prostate cancer (which clearly are not recognized in the medical art as being totally preventable conditions).

***Claim Rejections - 35 USC § 103***

Claims 1-4 and 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goulet et al. (US 5,981,550) in view of Onda et al. (US 5,677,184).

Goulet et al. teach a pharmaceutical agent comprising 1) an LHRH receptor agonist or antagonist in combination with 2) an androgen receptor agonist (testosterone) for use in men contraceptives (e.g., column 2, lines 17-22). Goulet et al. teach leuporelin is an LHRH receptor (e.g., column 2, lines 56-62). Goulet et al. do not teach the leuporelin specifically being leuporelin acetate.

Onda et al. teach that leuporelin acetate is a highly active derivative of LHRH (a superagonist), e.g., column 1, lines 59-67 and column 2, lines 1-10.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of Goulet et al. (column 2, lines 56-62) with using the acetate salt of leuporelin (leuporelin acetate) which was taught by Onda et al. to be a highly active derivative of LHRH (column 1, lines 59-67 and column 2, lines 1-10) with testosterone as androgen receptor agonist as taught by Goulet et al. The skilled artisan would have been motivated to do so because Goulet et al. teaches a combination of LHRH agonist(s) and testosterone as contraceptive in men and because leuporelin acetate is a superagonist of LHRH as taught by Onda et al. There would have been a reasonable expectation of success, given that Goulet et al. teach a combination therapy specifically comprising testosterone and an LHRH agonist such as leuporelin (e.g., column 2, lines 17-22 and claims). The pharmaceutical compositions of Goulet et al. in view of Onda et al. necessarily read upon the claims 6-7. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goulet et al. (US 5,981,550) in view of Onda et al. (US 5,677,184) and in view of Okada et al. (US 6,113,943).

Goulet et al. and Onda et al. are relied upon as before.

Goulet et al. teach sustained release compositions (e.g., at column 27, lines 1-4) but do not specifically teach long-term sustained release microcapsules that release the leuporelin acetate for not less than 2 months.

Okada et al. teach sustained-release microcapsules that release leuporelin acetate for not less than 2 months (e.g., column 1, lines 30-67 and column 2 lines 1-14; column 6, lines 10-14 and column 8, lines 65-67). The limitations of claims 9-10 are taught in Okada et al. (e.g., column 1, lines 30-67 and column 2 lines 1-14; column 6, lines 10-14 and column 8, lines 65-67) and a sustained release formulation (e.g., column 27, lines 1-4). Okada et al. teach that the sustained-release compositions

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the pharmaceutical composition of Goulet et al. by making sustained-release microcapsules of the highly active leuporelin acetate as taught by Onda et al. and by Okada et al. The skilled artisan would have been motivated to do so because sustained-release compositions, e.g., of leuporelin acetate have good dispersibility and workability and better storage stability (Okada et al. e.g., column 25, lines 59-65). There would have been a reasonable expectation of success, given that sustained release formulations of leuporelin acetate are taught and administered by Okada et al. (Example 2, column 22; Example 6, column 23 and Experimental Example 4, column 25) and because Goulet et al. teach sustained-release compositions are desirable (e.g., at column 27, lines 1-4) in the administration of compositions such as those comprising leuporelin and testosterone as taught above. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

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**Conclusion**

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

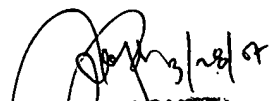
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Marcela M Cordero Garcia, PhD  
Patent Examiner  
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MMCG 03/07



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PRIMARY EXAMINER